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Pesticide Fact Sheet Number 183: Hexazinone

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This document contains up-to-date chemical information, including a summary of the Agency's regulatory position and rationale, on a specific pesticide or group of pesticides. A Fact Sheet is issued after one of the the following actions has occurred.

1. Issuance or reissuance of a registration standard,
2. Issuance of each special review document,
3. Registration of a significantly changed use pattern,
4. Registration of a new chemical, or
5. An immediate need for information to resolve controversial issues relating to a specific chemical or use pattern.

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Pesticides, regulations, Chemical Information Fact Sheet, Use Patterns, science findings.

b. Identifiers/Open-Ended Terms

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EPA

Pesticide Fact Sheet

Name of Chemical: Hexazinone
Reason for Issuance: Registration Standard
Date Issued: September 1988
Fact Sheet Number: 183

DESCRIPTION OF CHEMICAL

Generic Name: 3-cyclohexyl-6-dimethylamino-1-methyl-1,3,5-triazine-2,4(1H,3H)-dione

Common Name: Hexazinone

Trade Name: Velpar

EPA Shaughnessy Code: 51235-04-02

Chemical Abstracts Service (CAS) Number: 107201

Year of Initial Registration: 1975

Pesticide Type: Herbicide

Chemical Family: Triazine

U.S. Producer: Dupont

USE PATTERNS AND FORMULATIONS

Registered Uses: Terrestrial food crop use on fruit, sugarcane, alfalfa, pastures/rangeland and fallowland;

Terrestrial nonfood crop use on grasses, rights-of-ways, and other noncrop areas;

Aquatic nonfood crop uses on drainage ditch banks;

Forestry use on Christmas tree plantation, conifer release, and conifer forest plantings.

Predominant Uses: A selective herbicide used to control grasses and broadleaf and woody plants. Approximately 33% is used on alfalfa, 31% in forestry, 29% in industrial areas, 4% on rangeland and pastures, and < 2% on sugarcane.

Formulation Types Registered: Technical, formulation intermediate, granular, pelleted/tableted, dry flowable, emulsifiable concentrate, soluble concentrate/liquid, and ready-to-use liquid.

Methods of Application: Postemergence, preemergence, layby, directed spray, or basal soil treatment using ground equipment or where appropriate, broadcasted using aerial equipment.

Rates of Application: lb ai/A = pounds active ingredient per acre

Terrestrial food crop -	0.22 - 6.0 lb ai/A
Terrestrial nonfood crop -	0.67 - 13.5 lb ai/A
Aquatic nonfood crop -	1.0 - 13.5 lb ai/A
Forestry -	0.45 - 6.0 lb ai/A

SCIENCE FINDINGS

Chemical Characteristics:

Physical State: crystalline solid
Color: white
Melting point: 115-117°C
Solubility: soluble in water, chloroform, methanol, benzene, dimethylformamide, acetone, toluene, and hexane.
Vapor Pressure: 2×10^{-7} mmHg, 25°C.
Stability: Stable in aqueous solutions at pH 5, 7, 9 at temperatures up to 37°C.

Toxicology Characteristics:

Acute Toxicity:

Oral (rat): 1690 mg/kg (males), toxicity category III. Testing of females is required.

Dermal (rabbit): > 5278 mg/kg (males), toxicity category IV. If a gender difference is exhibited in the acute oral test on females, testing on females may be required.

Inhalation (rat): 7.48 mg/l (males), toxicity category III. If a gender difference is exhibited in the acute oral test on females, testing on females may be required.

Primary Eye Irritation (rabbit): Corrosive, causing irreversible eye damage, toxicity category I.

Primary Dermal Irritation: Not an irritant.

Subacute Toxicity:

A 21-day dermal study is required. Two acceptable oral toxicity studies were reviewed and no additional data are required. In the 90-day dog study, at the Lowest Effect Level (LEL) of 125 mg/kg (highest dose tested (HDT)), there was decreased body weight in both sexes, increased alkaline phosphatase in both sexes, decreased albumin /globulin values in both sexes, and increased absolute and relative liver weight in both sexes. There were no compound-related histopathological effects. The No Observed Effect Level (NOEL) was 25 mg/kg.

In the 90-day rat study, at the LEL of 250 mg/kg (HDT), there was decreased body weight in both sexes. There were no compound-related effects in mortality, toxic signs, food consumption, clinical pathology, organ weights, and histopathology. The NOEL was 50 mg/kg.

Chronic Toxicity:

Chronic Oral Toxicity: One acceptable chronic feeding study in rats has been submitted. A data gap exists for a chronic nonrodent (dog) feeding study.

In the rat study, there was increased survival over all test groups for male rats at 125 mg/kg at 2 years. Survival at 2 years in female rats was comparable between control and treated groups. The systemic NOEL was 10 mg/kg. At the LEL of 50 mg/kg, females had a 5% decreased body weight and slight decrease in food efficiency. At 125 mg/kg, there were significant toxic effects in both sexes. Males had a 12% body weight decrease, a 4% food consumption decrease, increased white blood cells and eosinophiles, alkaline urine and organ weight changes. Females had a 19% body weight decrease, slight food efficiency decrease, alkaline urine and organ weight changes.

Oncogencity: Mouse study - The oncogenic potential is inconclusive due to a possible ambiguity in the classification of liver neoplasia in both sexes. The systemic NOEL is 30 mg/kg. The liver slides must be rereviewed by the Agency.

Rat Study - There were no oncogenic effects up to and including 125 mg/kg (HDT).

The Agency will reassess hexazinone's oncogenic potential after rereview of the mouse study.

Teratology: Rat study - At 900 mg/kg/day (HDT), developmental toxicity was evidenced by decreased fetal body weight, and

partial ossification, kidney anomalies, and misaligned sternebrae. The LEL was 400 mg/kg and the NOEL was 100 mg/kg/day for developmental. For maternal toxicity, the NOEL was 100 mg/kg/day.

Rabbit study - NOEL for developmental and maternal toxicity was 50 mg/kg/day.

The Agency has determined that hexazinone is not a teratogen.

Reproduction: The Agency is requiring that additional information be submitted on a rat study that exhibited a NOEL of 50 mg/kg.

Mutagenicity:

Not a mutagen in a gene mutation, an unscheduled DNA synthesis or in a chromosomal aberration study in rats. However, a chromosomal aberration study with the Chinese hamster showed a positive response. The Agency has determined that hexazinone is not a mutagenic agent.

Metabolism:

The Agency has reviewed one acceptable rat metabolism study. C^{14} was excreted as an average of 97% of the total dosed radioactivity via the urine (ca. 77%) and feces (ca. 20%) during the collection period. The results were comparable for each treatment regimen. Very low levels of radioactivity were detected in the GI tract, hide, excised organs, muscle, blood, and fat. Hexazinone was metabolized primarily by hydroxylation and demethylation resulting in eight major metabolites. No additional data are required.

Major Routes of Exposure:

The major routes of exposure are dermal and ocular during mixing, loading, and application.

Physiological and Behavioral Characteristics:

Foliar Absorption: Hexazinone is absorbed through the roots and/or leaves depending upon the type of formulation and method of application.

Translocation: Following root absorption, hexazinone translocates upward through the xylem.

Mechanism of Pesticide Action: Hexazinone acts as photosynthesis inhibitor.

Environmental Characteristics:

Persistence in Water: Hexazinone is persistent in water at pH 5,7, and 9.

Mobility in soil: Hexazinone is mobile in soil.

Bioaccumulation: Hexazinone does not accumulate in fish.

Environmental Fate and Groundwater:

Contamination Concerns: Hexazinone belongs to the triazine family of pesticides. Some of these pesticides have been found in ground water. Because hexazinone has been identified as being persistent in water and mobile in soils, there is concern for groundwater contamination. Data are required to address this concern.

Nontarget Organisms: The Agency is requiring Droplet Spectrum and Spray Drift Evaluation tests because of the phytotoxicity of hexazinone, its aerial method of application, and the potential exposure of off-site plants to the pesticide.

Exposure of Humans:

Hexazinone has not been reported to be associated with any death or hospitalized cases since 1976. The voluntary accident reporting system reported one accidental ingestion.

Technical grade hexazinone is corrosive to the eye and causes irreversible eye damage. Use of protective goggles, face shield, or safety glasses are required for mixers, loaders, and applicators.

Exposure during Reentry Operations: The Agency has not received adequate toxicological or epidemiological evidence to indicate that residues of hexazinone can cause adverse effects on persons entering treated sites. No reentry data are required and no reentry interval has been imposed.

Ecological Characteristics:

LD = lethal dose
LC = lethal concentration
EC = effect concentration

Avian Toxicity: Acceptable data indicate that technical hexazinone is practically nontoxic to birds.

Acute oral (Bobwhite) LD_{50} = 2258 mg/kg
Dietary Toxicity (Mallard) LC_{50} = >10,000 ppm
(Bobwhite) LC_{50} = >5,000 ppm

Fish Toxicity: Acceptable data indicate that technical hexazinone is practically nontoxic to fish.

Fish Acute (Rainbow trout) LC_{50} = >320 ppm
(Bluegill sunfish) LC_{50} = >370 ppm
(Fathead minnow) LC_{50} = >274 ppm
(Bluegill sunfish) LC_{50} = >505 ppm

Freshwater Invertebrate Toxicity: Acceptable data indicate that technical hexazinone is practically nontoxic to freshwater invertebrates.

Daphnia magna EC_{50} = 145.3 ppm

Estuarine and Marine Organisms Toxicity: Acceptable data indicate that hexazinone is practically nontoxic to molluscs and slightly toxic to crustaceans.

Oyster 48-hr EC_{50} = >320 pm
Shrimp 96-hr LC_{50} = 78 ppm
Crab 96-hr LC_{50} = >1000 ppm

Nontarget Insects: There is insufficient information to determine that use patterns of hexazinone are nontoxic to honeybees. Therefore a honey bee acute study is required.

Potential Problems Related to Endangered Species: Because of the aerial use pattern of hexazinone on forests and/or rangelands, there is a threat to endangered plant species around these use sites.

Tolerance Assessment:

Tolerances Established: Tolerance regulations have been established for residues of hexazinone and its metabolites in a variety of commodities (refer to 40 CFR 180.396).

Results of Tolerance Assessment: The nature of the residue in plants is adequately understood. However, the metabolism of hexazinone in animals is not. Studies characterizing the total terminal residue of hexazinone in ruminants and poultry are required. Storage stability data and analysis of hexazinone residues on certain crops must be submitted. Additional residue analytical data are required. Processing data are needed for certain commodities. PHI's must also be established for some commodities. The adequacy of the established tolerances will be reassessed when the required data is reviewed.

SUMMARY OF REGULATORY POSITION AND RATIONALE

Hexazinone does not meet any of the criteria specified in 40 CFR 154.7; therefore a Special Review is not being initiated at this time.

The Agency will not require restricted use classification for hexazinone end-use products.

The Agency is not classifying hexazinone as an oncogen pending rereview of certain data from previously submitted studies.

Additional data are needed to thoroughly evaluate the potential of hexazinone to contaminate groundwater.

The Agency is requiring that a tolerance for pasture/ rangeland hay be proposed so that the impractical restriction against the cutting of hay from these sites be removed from the label.

The Agency is requiring that the tolerance for alfalfa hay be revised so that the impractical feeding restriction of alfalfa hay be removed from the label.

EPA is developing a program to reduce or eliminate exposure to endangered plant species from the use of hexazinone to a point where use does not result in jeopardy and will issue notice of any labeling revisions when the program is developed. Endangered species labeling is not required at this time.

While the data gaps are being filled, currently registered manufacturing-use products and end-use products containing hexazinone as the sole active ingredient may be sold, distributed, formulated, and used in the United States, subject to the terms and conditions specified in this Standard. Registrants must provide or agree to develop additional data, required in the Registration Standard.

STATEMENTS REQUIRED ON LABELS:

The following pesticide disposal statement must appear on hexazinone manfacturing-use products:

"Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or public waters unless this product is specifically identified and addressed in an NPDES permit. Do not discharge

effluent containing this product to sewer systems without previously notifying the sewage treatment plant authority. For guidance, contact your State Water Board or Regional Office of the EPA."

The Following Must Appear on End-Use Products:

In the Precautionary Statements:

"Corrosive, causes irreversible eye damage. Harmful if swallowed. Do not get in eyes or clothing. Mixers, loaders, and applicators must wear goggles, face shield, or safety glasses. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash before reuse."

Environmental Hazard Statement:

"Do not apply directly to water or wetlands (swamps, bogs, marshes, and potholes). Do not contaminate water when disposing of equipment washwaters."

In the Directions for Use Section:

"Do not enter or allow entry into treated areas until sprays have dried to perform hand tasks. A person may enter the areas to perform other tasks only if the person is wearing the personal protective eye equipment listed on the label."

As appropriate, the following grazing statements should appear on the label:

For sugarcane: "Do not feed sugarcane forage to livestock."

For conifer release and forest plantings (reforestation site preparation): "Do not graze domestic animals on treated areas within 30 days after treatment."

SUMMARY OF MAJOR DATA GAPS. The following data are required for hexazinone. Specific requirements are detailed in the Data Tables, Appendix I of the Hexazinone Registration Standard, which can be obtained from National Technical Information Service (NTIS) in Springfield, Virginia.

Study	Due Date - From Date of Standard
Product Chemistry	6 - 15 Months
Residue Chemistry	18 - 24 Months
Metabolism Studies	
Analytical methodology	
Magnitude of the Residue	
Storage Stability	
Toxicology	9 - 50 Months
Acute Oral	
Dermal Sensitization	
Subchronic 21 day Dermal	
Chronic Toxicity	
Ecological Effects	9 - 18 Months
Avian Reproduction	
Freshwater Fish LC_{50}	
Fish Early Life Stage	
Freshwater Invertebrate Acute EC_{50}	
Aquatic Invertebrate Life-Cycle	
Honey bee Acute Contact LD_{50}	
Environmental Fate	9 - 50 Months
Photodegradation	
Metabolism Studies	
Mobility Studies	
Soil Dissipation Studies	
Accumulation Studies (Irrigated crop and Rotational Crops)	
Spray Drift	
Groundwater Studies	

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DISCLAIMER: The information presented in this Pesticide Fact Sheet is for informational purposes only and may not be used to fulfill data requirements for pesticide registration and reregistration.